[0023] FIG. **8**: (A) SEC analysis of the interaction between C4 and hC4bNb6. (B) SEC analysis of the interaction between C4b and hC4bNb6. (C) SPR sensogram for apparent dissociation constant determination of C4:hC4bNb6. Full lines represent measured signal, dashed lines represent curve fit. (D) SPR sensogram for apparent dissociation constant determination of C4b:hC4bNb6. Full lines represent measured signal, dashed lines represent curve fit. (E) ka, kd and K_D values±S.E.

[0024] FIG. **9**: (A) SEC analysis of the interaction between C4 and hC4Nb8. (B) SEC analysis of the interaction between C4b and hC4bNb8. (C) SDS-PAGE analysis of the SEC analysis experiment between C4 and hC4Nb8 shown in panel (A) suggesting that hC4Nb8 binds weaker to C4 as compared to C4b since the nanobody is not apparent in the fractions containing C4.

[0025] FIG. **10**: (A) SEC analysis of the interaction between C4b and C2 in the presence of hC4bNb6 and SDS-PAGE of fractions. (B) SEC analysis of the interaction between C4b and C2 in the presence of hC4Nb8 and SDS-PAGE of fractions.

[0026] FIG. **11**. (A) Inhibitory action of hC4bNb6 and hC4Nb8 on deposition of C4b in a CP activation assay on a surface of deposited IgG. 59IF75 is C1q inhibitor IF75 described above. None of the nanobodies inhibits C4 deposition. (B) Inhibitory action of hC4bNb6 and hC4Nb8 on deposition of C3b in a CP activation assay on a surface of deposited IgG. 59IF75 is C1q inhibitor IF75 described above. Two additional C4/C4b specific Nbs, hC4bNb4 and hC4bNb5 are also inhibitory, but with lower efficacy as compared to hC4bNb6 and hC4Nb8. The C2 specific hC2NbG5 used here has little effect on CP C3 deposition

[0027] FIG. **12**. Bispecific C1q nanobodies and their ability to recruitment C1q and activate complement. (A) Constructs used in experiments. (B) Flow cytometry measurement of recruitment of C1q from human serum to Raji cells by BiCE161 (left). Incubation with BiCE161 results in complement activation and C3 deposition (right). Data are normalized. (C) Complement activation and C3 deposition by indicated bispecific nanobodies on EGFR expressing MDA-MB-468 cells. (D) Updated comprehensive version of FIG. **12**B. (E) Updated comprehensive version of FIG. **12**C.

[0028] FIG. **13**. Ability of DF85 and BiCE128 to recruit C1q and activate complement on different tumor cell lines. (A) Recruitment of C1q from human serum to MDA-MB-468, A431 and A1207 cells by DF85. (B) C3 deposition on MDA-MB-468, A431 and A1207 cells by DF85. (C) Recruitment of C1q from human serum to A431 and A1207 cells by BiCE161. (D) C3 deposition on A431 and A1207 cells by BiCE161. (E) Updated comprehensive version of FIG. **13**A. (F) Updated comprehensive version of FIG. **13**B. (G) Updated comprehensive version of FIG. **13**C. (H) Updated comprehensive version of FIG. **13**D.

[0029] FIG. **14**. Inhibitory action of pNSL270 on deposition of C3b in a CP activation assay on a surface of deposited IgG. IF75 is C1q inhibitor described above and pNSL157 is a control nanobody. As shown pNSL270 inhibits C3 deposition, and thus C3 cleavage, in a dose dependent manner upon activation of the classical pathway.

[0030] FIG. **15**. Inhibitory action of pNSL270 on deposition of C4b in a CP activation assay on a surface of deposited IgG. IF75 is C1q inhibitor described above and pNSL157 is a control nanobody. As shown pNSL270 does not inhibit C4b deposition and thus C4 cleavage.

[0031] FIG. **16**. SEC of the complex between mouse C4b (mC4b) and pNSL270 on a Superdex 200 Increase 10/300 column (left). SDS-PAGE of peak fractions 24+25 from run and pure mC4b and pNSL270 (right). As shown in the SDS-PAGE, pNSL270 binds to mouse C4b.

[0032] FIG. **17**. SEC of the complex between the globular head of human C1q (hC1qGH) and IF75 on a ENrich 70 10/300 column (left). SDS-PAGE of indicated fractions (right). As seen from the SDS-PAGE IF75 interacts specifically with the head region of hC1q.

[0033] FIG. **18**. Bio-layer interferometry (BLI) measurements of the interaction between hC1qGH and IF75. IF75 was immobilized on the sensors and numbers are concentrations of hC1qGH. Global fitting to the data shows that hC1qGH binds to IF75 with a dissociation constant of 0.5 nM.

[0034] FIG. **19**. Bio-layer interferometry (BLI) measurements of the interaction between hC1qGH and the bispecific nanobody pNSL161 composed IF75 linked to a CD38 specific nanobody. pNSL161 was immobilized on the sensors and numbers are concentrations of hC1qGH. Global fitting to the data shows that hC1qGH binds to pNSL161 with a dissociation constant of approximately 0.5 nM.

[0035] FIG. **20**. CVF-Bb cleavage assay. Cleavage of C3 into C3b in the presence or absence of DI62. DI62 inhibits the cleavage of C3 into C3b (generation of C3b alpha' chain) while the C3 is rapidly cleaved in the absence of the nanobody.

[0036] FIG. **21**. Fl mediate C3b cleavage assay. Cleavage of C3b by Fl in the presence or absence of DI62. As shown, DI62 does not inhibit Fl mediated C3b cleavage.

[0037] FIG. **22**. Surface Plasmon Resonance measurements of the interaction between DI62 and native C3, C3b and C3MA. DI62 binds with high affinity to both native C3, C3b and C3MA.

[0038] FIG. **23**. Effect of D121 and DI62 on C3d deposition in the alternative and classical pathways. (A) C3d deposition in the presence of control nb, D121 and hC3nb2 upon activation of the alternative pathway. D121 inhibits C3d deposition in a concentration dependent manner and DI62 inhibits at 10 μg/ml. (B) C3d deposition in the presence of control nb, D121 and hC3nb2 upon activation of the classical pathway. DI62 inhibit C3d deposition upon activation of the classical pathway while D121 and control nanobody have no effect on C3d deposition.

[0039] FIG. **24**. CVF-Bb mediated cleavage of native C3. Cleavage of C3 into C3b in the presence or absence of D121. D121 does not inhibit the cleavage of C3 into C3b (generation of C3b alpha' chain).

[0040] FIG. **25**. Fl mediate C3b cleavage assay. Cleavage of C3b by Fl in the presence or absence of D121. D121 inhibits Fl mediated C3b cleavage.

[0041] FIG. **26**. BLI competition experiment with between D121, mini-FH and FP for binding to C3b. D121 inhibits binding of hFP but not mini-FH to hC3b.

[0042] FIG. **27**. BLI measurements of the interaction between EWE-hC3nb1, C3 and C3b. EWE-hC3nb1 binds to hC3b but not hC3.

[0043] FIG. **28**. Fl mediate C3b cleavage assay. Cleavage of C3b by Fl in the presence or absence of EWE-hC3nb1. EWE-hC3nb1 inhibit Fl mediated C3b cleavage.